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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/323,738	06/01/1999	WILLIAM R. A. OSBORNE	P-UW-3570	9582

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 06/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/323,738	Osborne et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 11, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above, claim(s) *1-16 and 40* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-39* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's Remarks, filed 3/11/02, are acknowledged.

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 17-39 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of treating diabetes or forestalling a clinical symptom indicative of diabetes comprising implanting into an individual smooth muscle cells comprising a polyfluoroethylene prosthetic graft transfected with the vector/plasmid LhI*TgFuSN, does not reasonably provide enablement for:

a method of treating diabetes or forestalling a clinical symptom indicative of diabetes comprising implanting into an individual cells:

A) coexpressing proinsulin containing a proinsulin cleavage site,

B) coexpressing a glucose-regulated protease,

C) comprising a proinsulin cleavage site consisting of SEQ ID NO:7, for the reasons of record as set forth in Paper No. 12, mailed 9/19/01.

Applicant's arguments, filed 3/11/02, have been fully considered but they are not persuasive. Applicant argues that "even if one skilled in the art were to use a transfected β cell in the claimed methods and the alleged destruction were to occur, the implanted cells would not be prevented from ameliorating a clinical symptom of diabetes or forestalling a clinical symptom indicative of diabetes prior to destruction." It is the Examiner's position that said prevention or amelioration would indeed be forestalled as said transfected cells would be immediately attacked and killed be the previously primed autoreactive T cells. Applicant argues "Furthermore, if one skilled in the art were to use a transfected β cell in the claimed methods, those skilled in the art would have been able to increase the viability of the implanted cells according to the teaching and guidance in the specification." However, said guidance, e.g., the administration of immunosuppressive agents or the masking of surface molecules with antibodies, comprise unclaimed limitations.

Regarding Applicant's attempt to redefine "proinsulin," "Applicants respectfully submit that the term proinsulin as it is used in the claims and defined in the specification is consistent with the normal usage of the term in the art." It is the Examiner's position that "proinsulin," as use in the art, specifically defines the insulin precursor polypeptide consisting of an A, C, and B chain as set forth previously. It is improper to attempt to redefine the well-known polypeptide to include any and all recombinant analogs and "modified forms" that might be altered to encode a functional insulin.

Applicant argues that "The Office action alleges that the claims would not work with any glucose-regulated protease because not all proteases are capable of cleaving proinsulin. Applicant's respectfully submit that the claims are not directed to any glucose regulated protease but, as recited in the claims, to a glucose-regulated protease capable of cleaving the proinsulin cleavage site to produce insulin." It remains the Examiner's position that the furin construct disclosed in the specification is the single protease enabled by the specification that functions in the method of the instant claims. Applicant argues that "although Smeekins et al. describes the PC2 enzyme as being highly selective for the C-peptide-A-chain junction of rat proinsulin I and only producing low levels of mature insulin proinsulin I under their assay conditions, those skilled in the art would have recognized from the teaching and guidance in the specification that the PC2 enzyme can be used to produce mature insulin in the methods of the invention, for example, by incorporating the PC2 recognition site at both the C-peptide-A-chain junction and the B-chain-C-peptide junction." It is the Examiner's position that Applicant is again arguing unclaimed, and in this case, inadequately described limitations. Applicant's arguments that furin is "a glucose-regulated protease capable of cleaving the proinsulin cleavage site set forth in SEQ ID NO:7 to produce insulin," is not in dispute. It is the Examiner's position that furin is the only glucose-regulated protease enabled by the instant specification.

4. Claims 28-30 and 32-39 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons of record as set forth in Paper No. 12, mailed 9/19/01.

Applicant's arguments, filed 3/11/02, have been fully considered but they are not persuasive. Applicant argues that "The specification further describes a number of exemplary intermediates within the hexosamine biosynthetic pathway such as glucosamine-6-phosphate, glucosamine, N-acetyl glucosamine-6-phosphate, N-acetyl glucosamine-1-phosphate and UDP-N-acetyl glucosamine." The specification fails, however, to describe any hexosamine biosynthetic pathway *enzymes*, other than GFA. Applicant's description of an intermediate product is insufficient description of the enzyme responsible for the formation of said product.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
May 28, 2002

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600